

AMENDMENTS TO THE CLAIMS

The complete listing of all claims will serve to replace all prior versions of the claims.

Listing of claims

1. (Currently Amended) A method for the *in vitro* determination of cellular uptake of exogenous or endogenous substances in a cell sample, which method comprises:
 - 1) selecting a suitable shift agent (SA) able to induce LIS and nucleus combination for the measurement of cellular uptake of the exogenous or endogenous substance under investigation, through MAS-NMR spectroscopy, wherein said selection is carried out by:
 - a) identifying a set of possible SA candidates on the basis of the LIS produced on at least one NMR signal belonging to said exogenous or endogenous substance;
 - b) identifying a set of possible candidates for said SA, on the basis of the CC/s in which they distribute; and
 - c) selecting said SA and nucleus combination, on the basis of the information gathered from steps (a) and (b) ;
 - 2) determining the cellular compartment/s (CC/s) in which said exogenous or endogenous substance distributes, through MAS-NMR spectroscopy; and
 - 3) measuring the compartmental concentration of ~~the~~ said exogenous or endogenous substance.
2. (Canceled)
3. (Previously Presented) The method according to claim 1 wherein step 2) is carried out by:
 - d) acquiring the MAS-NMR spectrum of the *in vitro* sample containing the exogenous or endogenous substance under investigation and determining the marker^{EXO} or marker^{ENDO} signal/s;
 - e) adding a suitable amount of the selected SA to the above *in vitro* sample, so as to induce a significant LIS of marker^{EXO} or of marker^{ENDO} signal/s, and re- acquiring the same MAS-NMR spectrum; and
 - f) comparing the marker^{EXO} or the marker^{ENDO} signal/s of steps (d) and (e) and determining in which Cellular Compartment the exogenous or endogenous substance is present.
4. (Previously Presented) The method according to claim 1, where cellular uptake of exogenous substances is determined.

5. (Previously Presented) The method according to claim 4 wherein the exogenous substance is any substance not naturally occurring in a biological sample.
6. (Previously Presented) The method according to claim 5 wherein the exogenous substance comprises exogenous organic substances or exogenous metals or metal ions which NMR signals can be observed.
7. (Previously Presented) The method according to claim 6 wherein the exogenous substance is selected from the group consisting of: drugs for human and veterinary use, diagnostic and therapeutics agents, contrast agents for imaging techniques, radio-sensitizers for photodynamic and neutron capture therapy, pesticides, herbicides, fertilizers, food additives, preservatives, cosmetics, colorants, waste products, pollutants, and chemicals.
8. (Previously Presented) The method according to claim 1 wherein the endogenous substance comprises any substance resulting from normal or pathological biochemical processes of cells and tissues.
9. (Previously Presented) The method according to claim 8 wherein the endogenous substance is selected from the group consisting of natural carbohydrates, urea, lactate, citrate, acetate, carbonate, malonate, choline, creatine, phosphate, pyruvate and natural amino acids.
10. (Previously Presented) The method according to any one of claims 1 to 3, wherein the SA is selected from compounds containing a metal ion of the lanthanide group including: Ce^{3+} ; Pr^{3+} ; Nd^{3+} ; Pm^{3+} ; Sm^{3+} ; Eu^{3+} ; Tb^{3+} ; Dy^{3+} ; Ho^{3+} ; Er^{3+} ; Tm^{3+} ; and Yb^{3+} .
11. (Previously Presented) The method according to claim 10 wherein the SA comprises lanthanide complexes of ligands selected from: EDTA (ethylenediaminetetraacetic acid); PCTA (3,6,9,15-tetraazabicyclo-[9.3.1]-pentadeca-1(15)11,13-triene-3,6,9-tris (methane phosphonic acid)); BOPTA ((4RS)-[4-carboxy-5,8,11-tris (carboxymethyl)-1-phenyl-2-oxa-5,8,11-triazatridecan-13-oic acid]) or derivatives thereof; DTPA (diethylenetriamine pentaacetic acid) or derivatives thereof; DOTA (1,4,7,10-tetraazocyclo-dodecane-N,N',N'',N'''-tetraacetic acid) or derivatives thereof; DO3A (1,4,7,10-tetra azacyclododecane-1,4,7-triacetic acid) or derivatives thereof; DOTP (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetrakis (methane phosphonic) acid or derivatives thereof; and ([3 β (R),5 β ,12 α]-3-[[4-[bis(2-bis(carboxymethyl)amino)-ethyl]amino]-

4-carboxy-1-oxobutylamino]-12-hydroxycholesterol-24-oic acid).

- 12.** (Previously Presented) The method according to any one of claims 1 to 3, wherein the cell sample is selected from human or animal cells, cells cultures, tissues and organ cells, vegetal cells, part of trunks, leaves and food cells of both animal or vegetal origin.

Claims 13 – 14 (Canceled)